

REMARKS**Amendments to the Claims**

Claims 1-10 are pending.

Claims 1-10 have been amended.

Claim 1 has been amended to recite “one or more liquid or solid substances,” instead of “a fluid substance, and/or a substance comprised in a fluid substance.” Support for this amendment can be found in the Specification, for example, at page 10, line 31 through page 11, line 4; and page 22, lines 21-28.

Claim 1 has been amended to recite “a separation medium comprising a gas or liquid material.” Support for this amendment can be found in original Claim 4 and in the Specification, for example, at page 10, lines 10-21.

Claim 1 has been amended to recite “a connection medium comprising a liquid material by introducing said connection medium into the intermediate cavity.” Support for this amendment can be found in the Specification, for example, at page 10, line 22 through page 11, line 4 and at page 18, lines 24-30.

Claim 1 has been amended to delete all elements under step “c” and add the elements to the step “b.” Support for this amendment can be found in the Specification, for example, at page 10, line 22 through page 11, line 4 and at page 18, lines 24-30.

Claim 2 has been amended to recite “separating said one or more liquid or solid substances by applying a driving force selected from the group consisting of voltage, centrifugal force, capillarity, magnetic force, electroosmotic flow and mechanical pumping.” Support for this amendment can be found in the Specification, for example, at page 12, lines 10-14. Claim 2 has been amended recite “one or more liquid or solid substances” as in Claim 1.

Claim 3 has been amended to recite “one or more liquid or solid substances are separated by electrophoresis in the first and/or second cavities.” Support for this amendment can be found in the Specification, for example, at page 14, lines 7-20.

Claim 4 has been amended to recite “the separation medium is air” and “the connection medium is an electroconductive liquid solution, wherein said connection medium is introduced

into the intermediate cavity by capillarity.” Support for this amendment can be found in the Specification, for example, at page 26, lines 11-23.

Claim 5 has been amended to recite “said one or more substances whose transfer is to be controlled are liquid; the separation medium is a liquid material immiscible to said one or more liquid substances whose transfer is to be controlled; and said separation medium is introduced into the intermediate cavity by micropump or electroosmotic flow.” Support for this amendment can be found in the Specification, for example, at page 10, line 31 through page 11, line 4 and at page 18, lines 12-14.

Claim 6 has been amended to recite “one or more liquid or solid substances” as in Claim 1. Claim 6 has been amended to recite “receiving said one or more liquid or solid substances.” Support for this amendment can be found in the Specification, for example, at page 11, lines 21-22.

Claim 7 has been amended to recite “one or more liquid or solid substances by applying a driving force selected from the group consisting of voltage, centrifugal force, capillary, magnetic force, electroosmotic flow and mechanical pumping.” Support for this amendment can be found in the Specification, for example, at page 12, lines 10-14. Claim 7 has been also amended recite “one or more liquid or solid substances.”

Claim 8 has been amended to recite “first” and “second” electrophoretic medium to better clarify the claimed invention. Claim 8 has been also amended to recite “a separation medium comprising a gas or liquid material.” Support for this amendment can be found in original Claim 4 and in the Specification, for example, at page 10, lines 10-21. Claim 8 has been amended to recite “one or more proteins,” instead of “substances.” Support for this amendment can be found in the Specification, for example, at page 22, line 21 through page 24, line 26. Claim 8 has been also amended to add the phrase “and for holding a connection medium comprising a liquid material which allows transfer of said one or more proteins via the intermediate cavity.” Support for this amendment can be found in the Specification, for example, at page 10, line 22 through page 11, line 4 and at page 18, lines 15-30.

Claim 9 has been amended to delete the phrase “second cavity comprises the form of at least one groove or tube that branches from the first cavity” and to recite “connection medium is

introduced into the intermediate cavity via capillary action.” Support for this amendment can be found in the Specification, for example, at page 26, lines 11-24.

Claim 10 has been amended to better clarify the claimed invention. Claim 10 has been amended to add a step directed to “introducing one or more proteins to be electrophoresed into the first cavity of the electrophoretic device of claim 8.” Claim 10 has been also amended to recite “replacing a separation medium comprising air by introducing a liquid connection medium which allows transfer of said one or more proteins to be electrophoresed into the second cavity via the intermediate cavity of the electrophoretic device of claim 8.” Support for this amendment can be found in the Specification, for example, at page 5, lines 6-20.

No new matter has been added. Entry of these amendment is respectfully requested.

Amendments to the Specification

The Examiner has objected to the Specification for reciting hyperlinks. Applicants have deleted all hyperlinks from the Specification. The Specification has also been amended to correct obvious typographical errors. No new matter has been added. Entry of these amendments is respectfully requested.

Replacement Drawings

The Examiner has required new corrected drawings because the copies of the drawings are substantially illegible for the purpose of providing structural insight into the applicant's invention. Submitted herewith are copies of replacement drawings for Figures 1-3.

Rejection of Claims 1-10 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-10 have been rejected as being indefinite. The Examiner states that “It is unclear from the claims, as well as the specification, how the separation medium is to be replaced in the intervening cavity by the connection medium” (bridging paragraph of the Office Action at pages 2 and 3). As discussed above, Claim 1 has been amended to recite that “the separation medium” comprises “gas” or “liquid” and that “the connecting medium” comprises a “liquid” as originally set forth in Claim 4. Further, Claim 4 has been amended to recite that the separation medium is “air” and the connecting medium is “an electroconductive liquid solution.”

Claim 4 is also amended to recite that: “the connection medium is introduced into the intermediate cavity by capillarity.” Support for this amendment can be found in the Specification, for example, at page 26, last two paragraphs.

Unlike the statement by the Examiner,¹ the present Specification provides adequate written description for the mechanism by which a gaseous or liquid separation medium is replaced with a liquid connecting medium. For example, the Specification teaches the use of micropump and electroosmotic flow to replace the separation medium with the connection medium as shown below:

In the case where the separation medium is a liquid, this kind of procedure to introduce separation medium in to a capillary can be readily carried out by micropump or electroosmotic flow. (the Specification at page 18, lines 12-14; emphasis added)

The Specification also teaches the use of capillarity for replacing the separation medium with the connection medium as follows:

Aqueous solution is introduced to the capillary solely by capillarity, requiring no mechanical drive. Thus, this introduction can be accomplished extremely easily, reliably, and speedily. (the Specification at page 26, lines 21-24).

Accordingly, the present Specification provides adequate written description for the mechanism by which a gaseous or liquid separation medium is replaced with a liquid connecting medium.

The Examiner rejected independent Claim 1 and dependent Claims 2-4 as being indefinite for reciting “and/or.” Applicants have amended to delete “a fluid substance, and /or a substance comprised in a fluid substance” and to recite “one or more liquid or solid substances.”

Further, Claims 5 and 9 have been rejected as being indefinite for the phrase that the second cavity branches off from the first cavity when the intermediate cavity connects between the first and second cavities as in Claim 1. As noted above, Claims 5 and 9 have been amended to delete the phrase “the second cavity comprises the form of at least one groove or tube that branches from the first cavity,” rendering the rejection moot.

¹ “It is unclear from the claims, as well as the specification, how the separation medium is to be replaced in the intervening cavity by the connection medium” (Bridging paragraph between page 2 and page 3, Office Action).

Rejection of Claims 1-10 Under 35 U.S.C. § 103(a)

Claims 1-10 have been rejected as unpatentable over Lee *et al.* (U.S. Patent Application No. 2002/0170825; hereinafter, "Lee") in view of Hochstrasser *et al.* (U.S. Patent No. 4,874,490; hereinafter, "Hochstrasser"). The Examiner states that: "In view of HOCHSTRASSER, it would have been obvious to use the device of LEE in a similar way because that new use required no structural changes and ultimately performed the same function, simply in a different direction" (the Office Action at page 6).

As discussed above, independent Claims 1, 6, 8 and 10 have been amended. For the reasons set forth below, independent Claims 1, 6, 8 and 10, as amended, are not *prima facie* obvious over the references of record. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). Second, there must be a reasonable expectation of success. *Id.* The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. *Id.* Finally, the prior art references, when combined, must teach or suggest *all the claim limitations*. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

Lee teaches a method and microchannel device for two-dimensional electrophoresis. In Lee, the first dimension microchannels are physically joined to the second dimension microchannels in an orthogonal configuration (*see* Lee, Figures 2 and 3). The samples are transferred from the first dimension microchannels to the second dimension microchannels by changing electric potential from zero to a predetermined level. Because the first and second cavities are physically joined together in an orthogonal configuration (*see* Lee, Figure 1), Lee's device, as the Examiner correctly points out, does not facilitate the intermediate cavities. In Lee, samples are designed to be transferred from the first cavities to the second cavities by differential electric potentials. Thus, Lee's device does not teach or suggest the use of: (1) an intermediate cavity placed between the first and second cavities; (2) a separation or connection medium contained therein; and (3) replacing a gaseous or liquid separation medium with a liquid connection medium.

Hochstrasser teaches a system for two-dimensional gel electrophoresis, using two separate gels (*i.e.*, “strip gel” and “slab gel”) separated by an insulating (“separation medium”) layer that can be solid, liquid or gas (col. 2, lines 22-39). According to the teachings of Hochstrasser exemplified in Figure 3, the strip gel and the slab gel are separated by a space occupied by air. The first dimension of separation is permitted to occur on the strip gel with the air present in the space which prevents the transfer of samples. Once the desired separation is achieved in the first dimension, the two gels are placed in electrical contact for transfer from one gel to the other (col. 5, lines 3-24) either by: (1) pushing the first gel (“the strip gel”) until it physically comes in contact with the second gel (“the slab gel”) (*see*, col. 5, lines 25-30); or (2) introducing a new intervening gel between the first gel and the second gel (*see*, col. 5, lines 31-44). Hochstrasser does not teach or suggest the use of an liquid connection medium to allow the transfer of a sample from the first gel to the second gel as set forth in the present invention.

Lack of a Prima Facie Case of Obviousness

Independent Claims 1, 6, 8 and 10, as amended, are not *prima facie* obvious because: (1) the references of record, in combination, do not teach all elements of Claims 1, 6, 8 and 10, namely “replacing the separation medium comprising a gas or liquid by the connection medium comprising a liquid; and (2) one of ordinary skill in the art would not have been motivated to combine or modify the teachings of Lee and the teachings of Hochstrasser to arrive at the claimed invention.

Neither Lee nor Hochstrasser teaches or suggests the use of a connection medium comprising a liquid to replace the separation medium. As noted above, Lee’s device simply does not contain an intermediate cavity. Nor does it require the use of any medium comprising a liquid in such an intermediate cavity. Hochstrasser does not compensate for the deficiency. Hochstrasser does not teach or suggest the use of any liquid connection medium which facilitates the transfer of the samples from the first cavity to the second cavity. Hochstrasser merely teaches that, after adequate separation is achieved in the first gel, either the first gel can be physically pushed until it fully contacts the second gel (*see*, col. 5, lines 25-30) or a new gel can be introduced between the first gel and the second gel (*see*, col. 5, lines 31-44). Because the references of record do not teach or suggest all elements of independent Claims 1, 6, 8 and 10, as amended, these claims are not rendered obvious over the prior art references. Because

independent Claims 1, 6, 8 and 10 are not *prima facie* obvious, all claims dependent from these independent claims are not rendered obvious over the prior art references.

In addition, with respect to Claim 4, the Examiner states that: "...it would have been obvious to use a liquid as the [collecting] medium in the modified invention of LEE in view of HOCHSTRASSER because the continuity between the liquid of the first separation dimension and the [collecting] medium would make transport of the sample between the two much easier. Additionally, a liquid would allow for an electrical connection between the first and second gel dimensions as in HOCHSTRASSER" (the Office Action at page 8, first paragraph)

Applicants respectfully disagree. Absent impermissible hindsight, one of ordinary skill in the art would not have been motivated to modify the teachings of Lee and Hochstrasser to arrive at the present invention, namely using a liquid connection medium to facilitate the transfer samples.

First, Hochstrasser, the reference that the Examiner specifically relies on to find support for the elements relating to "intermediate cavity" and "separation and connection mediums," teaches the introduction of a new gel between the first gel and second gel. For the conventional size electrophoresis device, such as the one described in Hochstrasser, introducing a new gel between the two existing gels would have been a simple solution for placing the two gels in electrical contact for transfer. If a liquid medium was a possible option, Hochstrasser would have certainly suggested the use of a liquid connection medium. Hochstrasser, however, does not teach or suggest the use of the liquid connection medium because a liquid connection medium is not a feasible option for the conventional size electrophoresis device of Hochstrasser due to the distance that the sample must travel between the first gel and the second gel. At the time of the invention, one of ordinary skill in the art would have reasonably concluded that, for the conventional size electrophoresis device as shown in Figure 3 of Hochstrasser, introducing a new gel was a sufficient solution for making a electrical connection from the first gel to the second gel and would not have been motivated to modify the teachings of the prior art references and employ a liquid connection medium as in present invention.

Second, a 2-dimensional microchannel electrophoresis device, such as the one described in Lee, is designed to utilize a differential voltage in order to facilitate the transfer of samples from the first microchannels to the second microchannels without having to provide any

intermediate or intervening cavity (*see* Lee, Figure 6). Accordingly, the device does not provide any intermediate cavity, nor does it utilize a separation or connection medium to be held in the intermediate cavity. Lee does not teach or suggest any aspect relating to an intermediate cavity because Lee as well as one of ordinary skill in the art did not appreciate the problem associated two-dimensional microchannel electrophoresis device which allows contact and mixing of media for different dimensional electrophoreses that affects the electrophoreses conditions. It is Applicants who recognized this problem² and provide an effective solution by providing an intermediate cavity which alternatively holds a separation medium and a liquid connection medium. Without having to appreciate the problem, one of ordinary skill in the art would not have been motivated to modify the teachings of Lee or the teachings of Hochstrasser to arrive at the present invention.

In summary, the claimed invention is not obvious in view of the prior art references because the references of record, in combination, do not teach all elements of Claims 1, 6, 8 and 10, as amended; and (2) one of ordinary skill in the art would not have been motivated to combine or modify the teachings of Lee and the teachings of Hochstrasser to arrive at the claimed invention.

² “In these known microchips, electrophoretic separation is conducted within one continuous channel. Such a structure is not problematic, as long as the electrophoretic separation uses a single medium. However, it is difficult to use this same microchip structure in the continuous electrophoretic separation of combinations of different media. (the Specification at page 2, lines 21-24)

“In two-dimensional electrophoresis, electrophoresis must be carried out twice, using two different electrophoretic media” (the Specification at page 3, lines 10-11).

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By


Hak J. Chang

Registration No. 56,319

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

Concord, MA 01742-9133

Date:

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